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DOI: <https://doi.org/10.1093/eurheartj/ehr157>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-51130>

Journal Article

Accepted Version

Originally published at:

Ghadri, J R; Goetti, R; Fiechter, M; Pazhenkottil, A P; Küest, S M; Nkoulou, R N; Windler, C; Buechel, R R; Herzog, B A; Gaemperli, O; Templin, C; Kaufmann, P A (2011). Inter-scan variability of coronary artery calcium scoring assessed on 64-multidetector computed tomography vs. dual-source computed tomography: a head-to-head comparison. *European Heart Journal*, 32(15):1865-1874.

DOI: <https://doi.org/10.1093/eurheartj/ehr157>

Inter-scan variability of coronary artery calcium scoring assessed on 64-multidetector CT versus dual-source-CT: A head-to-head comparison

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Running title: Inter-scan Variability of Calcium Scoring: A Head-to-Head Comparison

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Word count: 2944

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Grants: The study was supported by a grant of the Swiss National Science Foundation (SNSF) and by the ZHIP (Zurich Center for Integrative Human Physiology, University of Zurich, Switzerland).

Abstract

Aims: Coronary artery calcium (CAC) scoring has emerged as a tool for risk stratification and potentially for monitoring response to risk factor modification. Therefore repeat measurements should provide robust results and low inter-scanner variability for allowing meaningful comparison. The purpose of this study was to investigate inter-scanner variability of CAC for Agatston-, volume- and mass scores by head-to-head comparison using two different cardiac computed tomography scanners: 64-detector multislice CT (MSCT) and 64-slice dual-source CT (DSCT).

Methods and Results: Thirty patients underwent CAC measurements on both 64-MSCT (GE LightSpeed XT scanner: 120kV, 70mAs, 2.5mm slices) and 64-DSCT (Siemens Somatom Definition: 120kV, 80 mAs, 3mm slices) within less than 100 days (0 - 97). Retrospective intra-scan comparison revealed an excellent correlation. The excellent intra-scan (inter-observer) agreement was documented by narrow limits of agreement and a correlation coefficient (COV) of $r \geq 0.99$ ($p < 0.001$) for all CAC scores with a low COV for both scanners (64-MSCT/64-DSCT), i.e. Agatston (2.0%/2.1%), mass (3.0%/2.0%), and volume (4.7%/3.9%). Inter-scanner comparison revealed larger Bland-Altman (BA) limits of agreement, despite high correlation ($r \geq 0.97$) for all scores, with COV at 15.1%, 21.6% and 44.9% for Agatston, mass and volume scores. The largest BA limits were observed for volume scores (-1552.8 to 574.2), which was massively improved (-241.0 to 300.4, COV 11.5%) after reanalyzing the 64-DSCT scans (Siemens) with GE software/workstation (while Siemens software/workstation does not allow cross vendor analysis). Phantom measurements confirmed overestimation of volume scores by “syngo Ca-Scoring” (Siemens) software which should therefore be reviewed (vendor has been notified).

Conclusion: Intra- and inter-scan agreement of CAC measurement in a given data set is excellent. Inter-scanner variability is reasonable, particularly for Agatston units

in the clinically most relevant range below 1000. The use of different software solutions has a greater influence particularly on volume scores than the use of different scanner types.

Word count: 301

Key Words: Coronary artery calcium score, Agatston score, volume score, mass score, cross vendor analysis, computed tomography, dual-source

Introduction

The incremental prognostic value of coronary artery calcium (CAC) scoring beyond conventional cardiovascular risk factors in different patient populations has been reported in a large number of studies.^{1, 2} As a consequence CAC has become increasingly important as a tool to detect atherosclerosis and guide the use of measures in prevention of future cardiac events particularly for relatively young and asymptomatic patients.^{3, 4} Due to its noninvasiveness the use of CAC as a tool for monitoring response to risk factor modification such as lipid lowering has been proposed more than a decade ago.⁵ The rapid technical advances in multislice computed tomography (MDCT) over the last years have led to a switch from the electron beam CT (EBCT) on which the CAC was originally introduced by Agatston et al.³ to CAC assessment by MDCT. Particularly, the early CT scanner generations have been extensively validated against EBCT.^{1, 6} An increasing number of patients is undergoing CAC scoring and potentially repeat scanning for treatment monitoring⁷⁻¹⁰ in different centers with a wide variety of CT scanners from different vendors despite the fact that evidence of supporting clinical monitoring by CAC scoring is lacking.¹¹ In order to allow meaningful comparison multi-institutional and multi-manufacturer international standards for quantification of CAC have been published by the Physics Task Groups of the International Consortium on Standardization in Cardiac CT.¹² As a majority of centers performing cardiac CT are now using 64-slice CT scanners, the knowledge of inter-scan variability of CAC obtained on this scanner generation from different vendors is crucial, but so far lacking. In particular, for comparison of data from 64-slice CT versus 64-slice Dual-Source CT (DSCT) only phantom data exist.¹³ Thus, the purpose of the present study was to evaluate the

head-to-head inter-scanner variability of CAC values obtained on a 64-slice MDCT scanner versus those obtained on a 64-slice DSCT scanner from a different vendor.

Methods

Study population

Thirty consecutive patients who underwent CAC measurements on both different CT scanners within an interval of 100 days were included in this study. The unenhanced CT scan for CAC scoring was obtained once from the attenuation correction scan at the occasion of a myocardial perfusion scintigraphy, which the other CAC scan was obtained as routine component of a CT coronary angiography. Thus, both CAC scans were obtained from clinically indicated routine examinations. Patients were retrospectively included in the study if they had signed informed consent authorizing their records to be included in our cardiac imaging research registry. Exclusion criteria were: arrhythmia, prior coronary artery bypass surgery or the presence of mechanical prosthetic valves, intracoronary artery stents, pacemakers and implantable cardioverter defibrillators. Before the study, a detailed interview was conducted to collect data on symptoms, previous cardiac events, and cardiovascular risk factors as summarized in Table 1.

CT data acquisition

CAC scanning was performed by non-contrast cardiac CT using a 64-slice MDCT scanner (LightSpeed VCT XT, GE Healthcare, Milwaukee, USA) and a 64-slice DSCT scanner (Somatom Definition, Siemens Healthcare, Forchheim, Germany). All scans were performed in cranio-caudal direction during inspiratory breathhold with prospective electrocardiogram (ECG)-triggering as previously reported.¹⁴ ECG triggering was set at 75% of the RR-interval without padding for both scanners. The detailed acquisition parameters according to the respective vendors' recommendations for each scanner are given in Table 2. The calcium scores

obtained with the two different scanners and respective scanning parameters were validated by phantom measurements. A commercially available anthropomorphic cardio CT phantom, established and proposed by the Physics Task Group of the International Consortium on Standardization in Cardiac CT (in close collaboration with the vendors (GE Healthcare, Philips Medical Systems, Siemens Medical Solutions and Toshiba Medical Systems)¹², consisting of a body (QMR-Thorax, QRM, Moehrendorf, Germany) - with artificial lungs and a spine insert surrounded by soft tissue equivalent – and a cardiac calcification calibration insert (QRM-CCI, QRM, Moehrendorf, Germany) containing nine cylindrical calcifications of different size and hydroxyapatite density was examined with both scanners using the same acquisition parameters as for the patient study.^{12, 15-17}

CT data evaluation

All CAC datasets were analysed in random order by two blinded independent observers, each with 3 years of experience in cardiac imaging, using commercially available software packages of each respective manufacturer (“SmartScore”, GE Healthcare, Milwaukee, USA and “Syngo CaScore”, Siemens Healthcare, Forchheim, Germany). CAC scores were separately obtained for each of the main epicardial coronary arteries (left main artery (LMA), left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA))¹⁸ and summed to obtain total CAC. For every patient, CAC values were calculated using three different algorithms according to the recommendations for standardization from the above-mentioned Consortium¹² yielding the Agatston-³, volume-¹⁹ and mass scores.²⁰ Details of these algorithms have been described extensively elsewhere.^{12, 21} Briefly, their respective formulas are as follows:

$$\text{Agatston score} = \text{slice increment/slice thickness} \times \sum (\text{area} \times \text{cofactor})$$

Mass score = Σ (area x slice increment x mean CT density) x calibration factor

Volume score = Σ (area x slice increment)

Σ includes the sum of the values in parenthesis obtained from each individual lesion.

For the phantom study six different cylinders of two sizes (3x3mm and 5x5mm) and three different hydroxyapatite (HA) densities (200 mg/cm³ HA, 400 mg/cm³ HA and 800 mg/cm³ HA) were scored using the same software packages as for the patient study.¹²

Cross vendor analysis

All images acquired on the 64-DSCT (Siemens) were transferred to the GE workstation/software to obtain a cross-vendor analysis of Agatston, mass and volume scores. Conversely, Siemens workstation/software does not allow analysing data from GE scans. .Therefore we could only perform cross vendor analysis of 64-DSCT (Siemens) data on GE software (but not vice versa).

Image quality assessment

The image quality of CAC scans regarding motion artefacts was visually assessed for each coronary artery on a 5-point scale as previously reported²² : 1, no motion artefact; 2, minor artefact (slight blurring in less than half of the course of the vessel); 3, moderate artefact (severe blurring or double-imaged structures in more than half of the course of the vessel); 4, severe artefact (doubling and blurring over the whole course of the major vessel); 5, non-diagnostic (vessel structures not differentiable).²²

The LMA was assigned to the LAD vessel.

In addition, image noise was measured by one observer not involved in the image quality or reproducibility assessment. It was defined as the standard deviation of

attenuation measured in a region of interest (ROI) that was placed in the ascending aorta at the level of the coronary ostia. The ROI was chosen as large as possible, excluding the vessel wall to avoid partial volume effects.

Radiation dose estimation

Values for effective radiation dose were calculated by multiplying the dose length product (DLP) with a conversion factor ($k = 0.014 \text{ mSv/mGy} \times \text{cm}$) as previously described²³ and adopted in large trials.²⁴

Statistical analysis

Statistical analysis was performed using SPSS software (18.0, SPSS inc., Chicago IL, USA). Quantitative variables were expressed as mean \pm standard deviation (SD) or median (range) as appropriate, and categorical variables as frequencies or percentages. Differences in total Calcium scores (for Agatston, mass, and volume scores) regarding intra-, inter-observer and inter-scan comparison were analysed by Wilcoxon signed ranks test. To assess intra-observer variability, each reader evaluated all datasets twice after a minimum delay of two weeks. Inter-scan agreement was performed by comparing CAC obtained on the two scanner types in each patient. Intra- and inter-observer variability as well as inter-scan agreement were assessed using Spearman's correlation and Bland-Altman (BA) analysis with limits of agreement as previously reported.²⁵ Data were log (\log_{10}) transformed to reduce skewness of the given values and used to show regression analyses. The coefficient of variation (COV) was calculated as SD/mean and expressed as a percentage for better comparison of the values. The standard error of the estimates was assessed to characterize the linear fit of the data.

Image quality was correlated to the mean heart rate and differences in image quality between 64-MDSCT and 64-DSCT were assessed using Chi-square test. Differences in image noise were tested with Wilcoxon signed rank test and the influence of body mass index (BMI) on image noise was evaluated by regression analysis. All *P* values were two-sided and a *P* value <0.05 was considered statistically significant.

Results

Study population

Thirty patients (7 female, age 71 ± 8 years, BMI: 25 ± 4 kg/m²) underwent successful scanning on both scanner types (64-MDCT and 64-DSCT) within 23 ± 27 days (range 0 - 97 days) and were included in the present study. The patient baseline characteristics are listed in Table 1. The sequence of CAC scanning was: 64-MDCT first in 19 patients, and 64-DSCT first in 11 patients. None of the patients received intravenous beta-receptor antagonists prior to the scan.

Phantom study

Calcium scores of the six inserts obtained with the two scanners in the phantom were nearly identical regarding Agatston score (64-DSCT: 695; 64-MDCT: 690) and highly accurate for the mass scores (calibrated phantom mass: 167 mg; 64-DSCT: 167 mg; 64-MDCT: 165 mg) (Table 3). However, while volume scores from 64-MDCT were slightly underestimated for low density lesions, volume scores from 64-DSCT were highly overestimated for intermediate and high density lesions. Thus, the differences in volume scores could be largely attributed to the software used for CAC scoring rather than the scanner.

In fact, when the volume scores from 64-DSCT Siemens scanner and Siemens software were recalculated by the GE software the values were substantially closer to the phantom values (Table 3), indicating that not the Siemens scanner but rather the quantification algorithm in the Siemens software “syngo CaScoring” accounted for the inaccurate volume score measurements in intermediate and high density lesions (Figure 4).

Intra-scan comparison: Intra- and Inter-observer variation

Intra- and inter-observer agreements of Agatston, mass, and volume scores were excellent for both scanner types as evidenced by strong and significant correlations with narrow limits of agreement (Table 4).

Inter-scanner comparison

For all inter-scanner CAC measurements results are summarized in Table 5 and illustrated in Figure 1. Inter-scanner comparison for Agatston scores revealed an excellent correlation ($r = 0.976$, $P < 0.01$), despite relatively wide limits of agreement and a COV of 15.1%. Mass score comparison between the two scanners also revealed excellent correlation ($r = 0.975$, $P < 0.01$) with a COV of 21.6%. Although, inter-scan correlation of volume scores was also excellent ($r = 0.971$, $P < 0.01$), BA analysis revealed wide limits of agreement and a substantial bias towards lower values from 64-MDCT compared to 64-DSCT resulting in high COV 44.9%.

Cross vendor analysis

Interestingly, by use of GE software for Siemens scans the COV decreased substantially compared to original analysis for the Agatston (10.4% vs. 15.1%), mass (16.5% vs. 21.6%) and particularly for volume (11.5% vs. 44.9%) scores. (Table 5 and Figure 2 and 3).

CAC image quality

There was no significant difference in image quality between the two scanners (Figure 4) for any of the coronary vessels and for the overall image quality (Table 6). However, overall image quality tended to be superior in 64-DSCT. Diagnostic image

quality was found in all 64-DSCT and 64-MDCT scans. For both scanners image quality was significantly inferior in the RCA vs. LCX. ($P < 0.05$).

Image noise tended to be lower in 64-MDCT compared to 64-DSCT ($21.0 \text{ HU} \pm 6.6 \text{ HU}$) vs. ($23.4 \text{ HU} \pm 6.6 \text{ HU}$) without reaching statistical significance ($P > 0.067$).

Regression analysis showed a statistically significant influence of the patient's BMI on image noise for both scanner types ($P < 0.05$).

Radiation dose

The average DLP was $73 \pm 28.6 \text{ mGy} \times \text{cm}$ (effective dose: $1 \pm 0.4 \text{ mSv}$) on 64-MDCT, and $65.7 \pm 33.1 \text{ mGy} \times \text{cm}$ (effective dose: $0.9 \pm 0.5 \text{ mSv}$) on 64-DSCT respectively (n.s.).

Discussion

The present study reports an excellent intra- and inter-observer reproducibility and a good inter-scanner agreement of coronary CAC assessment between a 64-slice MDCT and a 64-slice DSCT scanner from two different vendors, with decreasing agreement at increasing calcium scores.

The Multi-Ethnic Study of Atherosclerosis (MESA) has also evaluated inter-scan variability and provided repeatability limits.^{6, 26} These limits are important in order to evaluate whether an increase in CAC score exceeds that expected from natural progression or that of measurement error alone.²⁷ The present study confirms an excellent intra- and inter-observer reproducibility of CAC on each scanner. For all scores including Agatston-, volume- and mass scores across a wide range of CAC values. The present data on intra- and inter-observer reproducibility are in line with previous findings.²⁸

Our study is the first to report a head-to-head inter-scanner comparison between two of the most widely used scanner types. Only few studies have reported similar comparisons^{29, 30} and these comparisons were made by using techniques which are now outdated. For Agatston scores we found a COV of 15.1% comparing well to the values reported in the literature (19-37%).

^{19, 20, 31-33}. Inter-scanner variability for mass score was 21.6% while it was substantially higher for the volume scores (44.9%) despite similar intra- or inter-observer variability for this measurement. Interestingly, when recalculating CAC from 64-DSCT scans (Siemens) using the workstation/software of the other vendor (GE), there was a significant decrease in volume scores, resulting in a substantial reduction of the COV to 11.5%. Although our results suggest that accurate and reliable CAC data can be obtained from both scanners values of volume scores differ significantly

from the two vendors, mainly due to differences in the quantification algorithm although differences in slice thickness may lead to differences in partial volume artefact affecting predominantly the volume score.

The phantom measurements revealed a slight underestimation (-30%) of volume scores in low density lesions by GE software/workstation. By contrast, a massive overestimation of volume scores has been found in intermediate (+100%) and high density lesions (+159%) by Siemens software/workstation (Figure 3) which should therefore be reviewed (vendor has been notified).

From the BA plot for Agatston scores it can be concluded that despite a good correlation over the whole range of values the agreement is best for values below 1000, while it decreases in patients with extensive calcifications. This is important because absolute precision of repeat measurements appears most relevant in patients without excessive calcifications, in whom risk factor modification may slow progression and therefore its monitoring may be appropriate. The volume score has been suggested as a favourable alternative to the traditional Agatston score as it allows robust assessment of the extent to which the volume of atherosclerosis plaque may decrease, stabilize or increase using lipid lowering treatment.^{5, 20}

The multimanufacturer international standards for CAC measuring¹² may have, at least in part, contributed to the robustness of such measurements even in cross-vendor comparison. This now allows tracking atherosclerosis progression on different scanners from different vendors^{19, 20} although accuracy of the results calculated from various types of software on different workstations may require validation against a reference phantom. Whether the variance of measurements as evidenced in the present study allows obtaining clinically acceptable results will remain a matter of clinical judgement in each study setting. Across the literature progression of CAC score is generally given as percent change from the baseline value because greater

absolute changes are observed in patients with higher baseline scores in whom even large CAC increase does not necessarily reflect a pronounced clinical deterioration.²¹
³⁴⁻³⁸ Raggi et al. have suggested a change >15% for Agatston score within one year as a clinically meaningful progression.³⁴ In fact, relatively large increases in CAC in patients with extensive calcifications do not necessarily reflect a pronounced clinical deterioration.²⁰

The inter-scanner COV for Agatston scores (15.1%) lies substantially below the typically reported values of the annual CAC progression rates of 20% to 24% per year.²¹ Thus, while intervals shorter than 1-2 years may be of questionable value,^{11, 39} monitoring CAC progression over time does not necessarily require the repeat scan being performed on the same device of the same vendor. At present, an individualized algorithm, rather than a systematic performance of serial CAC measurement seems appropriate based on the existing evidence.³⁹

Study Limitations

First, we do not have data on repeat measurements on the same scanner which would directly support the notion that rescanning should be performed on the same scanner for obtaining optimal agreement, although published data seem to suggest this.⁴⁰ However, such analysis was beyond the scope of the present study because it would require 4 scans per patient, i.e. two scans in each subject with each scanner. Second, in the present study, no systematic use of beta blocker for heart rate regulation and slowing was implemented. Although this may account for some part of the inter-scan variability, the fact that each patient served as his own control may have counterbalanced this drawback strengthening the validity of our data. In this context it should be emphasized, that the design of the present study does not allow evaluating systematic technology related biases towards higher accuracy of one type

of scanner over the other. This is particularly true for Agatston score which represents a mathematical construct and therefore cannot be compared to a physical standard of reference in contrast to mass and volume scores.

Finally, the median Agatston score was over 750 indicating that the patients represent a high risk population which potentially limits the generalizability of our results. On the other hand, however, inclusion of many patients without coronary calcifications would have added only limited information to CAC comparability. We therefore, felt it preferable including a wide range of CAC (0-5156 Agatston score).

Conclusion

Intra-scanner variability (intra- and inter-observer comparison of CAC scoring in a given data set is excellent. Inter-scanner variability is reasonable, particularly for Agatston scoring in the clinically most relevant range below 1000. The use of different software solutions for CAC scoring has a greater influence on volume scores than the use of different scanner types.

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Figure Legends

Figure 1 Inter-scanner correlations (left panel, logarithmic scale) and Bland-Altman limits of agreement (right panel) are given for Agatston (A), mass (B), and volume score (C). Scans were analyzed by dedicated software and workstation from scanner vendor as for scanner on which data was acquired. AU indicates Agatston Units.

Figure 2 The reanalysis of Siemens scans by GE software/workstation eliminates the variability introduced by differences in dedicated software/workstation. This is illustrated by narrowing of Bland Altman limits of agreement compared to Figure 1 for Agatston (A), mass (B), and most impressively for volume score (C). As GE data and Siemens software are not compatible no such cross-vendor analysis is available.

Figure 3 In intermediate ($400\text{mg}/\text{cm}^3$) and high density ($800\text{mg}/\text{cm}^3$) lesions 64-DSCT (Siemens) substantially overestimates the volume scores, while 64-MDCT (GE) slightly underestimates volume scores in low density lesions ($200\text{mg}/\text{cm}^3$) compared to calibrated phantom which has been previously established.¹²

Figure 4 Axial images demonstrating calcifications in all three epicardial vessels of a 70-year old patient with equal image quality from nonenhanced 64-MDCT (GE) (A) and from 64-DSCT (Siemens) (B).

Acknowledgment

We gratefully thank Patrick von Schulthess for excellent image reconstruction. as well as to Ennio Mueller, Edlira Loga, Rosanna Amore, Sabrina Epp, Mirjam De Bloeme and Desirée Beutel for their excellent technical support.